DATE 30 Sep 03

USAMMDA INFORMATION PAPER

PRODUCT: MALARIA RECOMBINANT VACCINE (RTS,S)

DESCRIPTION: The candidate *Plasmodium falciparum* malaria vaccine consists of the RTS,S recombinant protein antigen combined with a proprietary adjuvant system known as ASO2. The RTS,S antigen, produced in yeast cells, consists of two proteins, RTS and S, that spontaneously assemble intracellularly into mixed particles that each contain approximately 100 polypeptides. RTS is derived from a sporozoite surface antigen from the malaria parasite, fused to a small portion of the Hepatitis B virus S protein. The RTS,S vaccine and the AOS2 adjuvant system are both manufactured by GlaxoSmithKline Biologics. Malaria is endemic in virtually all tropical and subtropical regions of the world. Of the four human varieties of malaria, *P. falciparum* malaria is the most life threatening. After infection, *P. falciparum* causes massive destruction of red blood cells. Severe complications result when infected red blood cells block capillaries, hampering blood flow to vital organs like the brain, liver, kidneys and lungs. If untreated, acute *P. falciparum* malaria can progress very rapidly and death can occur within a few days. The World Health Organization estimates that between 300 and 500 million cases of malaria occur per year worldwide and that malaria causes between 1.5 and 2.7 million deaths. Resistance to antimalarial drugs is widespread and strains of *P. falciparum* resistant to several drugs have appeared in parts of Asia and Africa, thus making the development of a vaccine even more critical. *P. falciparum* malaria can rapidly incapacitate large numbers of personnel and has the potential to cause large numbers of casualties whenever U.S. Forces operate in endemic areas.

PROGRAM RELEVANCE to the ARMY: This vaccine supports both the core mission of the Army and the Army Transformation. Of the Army's core competencies, this product supports: "Shape the Security Environment," "Mobilize the Army", "Forcible Entry Operations," "Sustained Land Dominance" and "Support Civil Authorities" by protecting U.S. Forces against malaria caused by *Plasmodium falciparum*. The RTS,S vaccine will enhance the survivability and sustainability of U.S. Forces in regions of the world where malaria caused by *P. falciparum* is endemic. In addition, this product supports Future Operational Capability MD97-007 (Preventive Medicine).

ISSUES/ ACTIONS:

- In an effort to enhance the immunogenicity and duration of protection, the RTS,S vaccine will be combined with a new, proprietary adjuvant system (AS01B) and evaluated in a Phase 1/2a safety, immunogenicity and preliminary efficacy trial in U.S. volunteers. An Investigational New Drug application to cover this vaccine-adjuvant formulation was filed with the FDA in 4QFY03. A request to reschedule Milestone B to 1QFY08 has been submitted to reflect the delays due to incorporation of the new adjuvant.
- A multi-staged, multi-antigen vaccine may be necessary to attain the desired level and duration of protection. A Phase 1 safety, immunogenicity and preliminary efficacy trial in U.S. volunteers will test a mixture of RTS,S and a recombinant malaria protein antigen (AMA-1) derived from a different stage of the malaria parasite (the merozoite stage). The trial of the mixture awaits successful completion of a Phase 1 study of the AMA-1 vaccine alone, scheduled for 1QFY04.

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DA PROJECT/TASK: Infectious Diseases
PE/PROJ 643807.808ND
MAMP RANK: 7/36
ARMY ORD: *P. falciparum* Vaccine; CARDS # 1296; 13 Mar 97

SCHEDULE:

MS I	4QFY96
MS B	1QFY08
MS FRP	4QFY08

For additional information, contact: Pharmaceutical System Division, DSN 343-2051, Comm. 301-619-2051